PATENT COOPERATION TREATY

PCT

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference L/2BI14/1P	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/010983	International filing date *(day/month/year)* 28.09.2004	Priority date *(day/month/year)* 03.10.2003
International Patent Classification (IPC) or national classification and IPC A61K31/405, C07D209/18, A61P5/00, A61P37/02		
Applicant VEIJLEN N.V.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.08.2005	16.03.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Papathoma, S Telephone No. +49 89 2399-7536

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/010983

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-25 as originally filed

   Claims, Numbers

   1-15 received on 03.08.2005 with letter of 02.08.2005

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-15

because:

☒ the said international application, or the said claims Nos. 7 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-15 are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-15
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-6,8-15
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 7 relates to a method of improving the immunity of a non-human animal. Due to:
a) the reference in page 7, lines 4-5 to the effect of the claimed composition in reducing the death rate of said animals caused by **diseases**,
b) example 5 referring to the treatment of piglets having a Staphylococcus infection,
c) claim 8 referring to "**therapeutical** compositions for stimulating the immune system" and
d) claim 12 referring to "animals having a growth deficit and/or weakened immune system" thus to non-healthy animals,
claim 7 is considered to have a therapeutical aspect and thus its subject-matter is considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).
Claim 7 could be considered as a non-"method of treatment"-claim, only in the case that it was clear, that this method were to be applied in healthy animals.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: PATENT ABSTRACTS OF JAPAN vol. 2003, no. 02, 5 February 2003 (2003-02-05) & JP 2002 281914 A (NISHI NIPPON GREEN KK), 2 October 2002 (2002-10-02)

D2: PATENT ABSTRACTS OF JAPAN vol. 009, no. 331 (C-321), 25 December 1985 (1985-12-25) & JP 60 161920 A (MASAKI KAMATA), 23 August 1985 (1985-08-23)

D3: PATENT ABSTRACTS OF JAPAN vol. 010, no. 056 (C-331), 6 March 1986 (1986-03-06) & JP 60 199801 A (MASAKI KAMATA), 9 October 1985 (1985-10-09)

D4: PATENT ABSTRACTS OF JAPAN vol. 2000, no. 16, 8 May 2001 (2001-05-08) & JP 2001 026579 A (KOBE TENNENBUTSU KAGAKU KK; JAPAN SCIENCE & TECHNOLOGY CORP), 30 January 2001 (2001-01-30)

The application refers to an **animal feed composition** comprising free **IAA** or a derivative thereof capable of stimulating growth or the immune system in animals.

1) Article 33(2) PCT

Document D1 refers to a method for producing nutrient vitality promoter for fishes and livestock comprising indoleacetic acid. D2 refers to a growth agent for animal containing a plant growth hormone eg. oxyauxin such as oxyindoleacetic acid. D3 discloses a method for administering plant growth hormone eg. auxin (IAA) to an animal.

However, a minimum quantity of 240 microgram of IAA or a derivative thereof per kilogram of feed composition is not disclosed in any of these documents. The subject matter of the present application can thus be considered to fulfill the requirements of Article 33(2) PCT.

2) Article 33(3) PCT

The technical problem underlying the present application is the provision of an animal feed composition capable of increasing the growth rate and/or improving the feed efficiency and/or the feed conversion rate and/or the immunity of an animal. It is also directly claimed the use of IAA or a derivative thereof for the preparation of a therapeutical composition for stimulating the immune system of non-human animals (claim 8).
Although the prior art disclosed the use indoleacetic acid for enhancing growth in animals as well as its nutritional aspect (D1), there was no indication for the stimulating aspect of IAA or a derivative thereof on the immune system of the animals.
The subject matter of the present application can thus be acknowledged as inventive according to Article 33(3) PCT.

3) Article 34(4)(a)(I) PCT / Rule 67.1(iv) PCT

For the assessment of the present claim 7 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

a) The relevant background art disclosed in the documents D1-D3 is missing from the description (Rule 5.1(a)(ii) PCT).

b) The formulation of claim 9 corresponds to a second medical use claim. However, the stimulation of growth can not be considered as a therapeutical application.

Re Item VIII

Certain observations on the international application

1) Claim 1 and subsequently following claims referring to claim 1, do not fulfill the requirements of Article 6 PCT:

a) Claim 1 is an "open-ended claim". Although the minimum concentration of IAA or a derivative thereof is defined, no reference is made in claim 1 regarding its maximum concentration. Such a reference is only to be found in the dependent claim 2. Subsequently, claim 1 may refer to concentrations more than 40g of free IAA or a derivative thereof, such as eg. 999g. For such high concentrations it is however questionable if the technical problem can be solved (Article 33(3) PCT).

b) The essential feature of the claimed feed compositions is a minimum concentration of free IAA or a derivative thereof of 240 microgram per kilogram. This is also the feature that differentiates the present application from the prior art. However, 240 microgram of a derivative of IAA would lead -after conversion- to a lower quantity of IAA.

c) The definition of the derivative as "a compound that can be converted into free IAA in 3, preferably in 2 and more preferably in 1 step":

I) is a functional definition

ii) it does not make clear which compounds are covered by the scope of the claim. The reference to Bartel et al. is not sufficient as to clarify which compounds are meant. For example, according to Bartel et al. indole is converted in at least 4 steps to IAA. In D4, however, indole is converted in 3 steps to IAA. It is therefore not clear if indole will be comprised within the scope of the claim.

iii) the wording "preferably" has no limiting effect on the scope of the claims. The features following these expressions are therefore superfluous, thereby resulting in a lack of conciseness of the claim.

2) The concentration of free IAA or a derivative of 240 microgram till 40 gram per kilogram may be considered as broad for the claimed effect.

3) The reference in claim 4 to "an enzyme capable of converting the derivative into free

IAA" is objected under Article 6 PCT.

4) Claim 5 can not be considered as clear. In the originally filed claims this claim was referring to the aromatic ring of 4-hydroxy-IAA etc.. However in the amended set of claims this reference point is missing, while the dependancy on claim 4 is considered as incorrect.

5) As mentioned under Point VII, the formulation of claim 9 corresponds to a second medical use claim. However, the stimulation of growth can not be considered as a therapeutical application.

6) Claim 10 is a "result-to-be-achieved" claim.

7) Claim 15 referring to a "method of raising non-human animals" is objected under Article 6 PCT.

8) The reference to "animal" in claims 9-15 includes also human beings.

AMENDED CLAIMS (65)

1. An animal feed composition comprising more than 240 microgram of free IAA or a derivative thereof per kilogram, wherein said derivative is selected from the group consisting of 4-hydroxy-IAA, 4-methoxy-IAA, 5-hydroxy-IAA, 5-methoxy-IAA, 6-hydroxy-IAA, 6-methoxy-IAA, 7-hydroxy-IAA, 7-methoxy-IAA and a compound that can be converted into free IAA in 3, preferably in 2 and more preferably in 1 step.

2. A feed composition according to claim 1 comprising up to 40 g of free IAA or a derivative thereof per kilogram.

3. A feed composition according to claims 1 or 2 comprising between 100 and 1000 mg of free IAA or a derivative thereof per kilogram.

4. A feed composition according to claims 1 to 3 additionally comprising an enzyme capable of converting the derivative into free IAA.

5. A feed composition according to claim 4 comprising an aromatic ring wherein the aromatic ring is substituted on one or more of the 4, 5, 6 and 7 position with methyl, amino, nitro, fluoride, chloride, bromide or iodide.

6. A feed composition according to claims 1 to 5 in the form of pellets, meal, grains, extruded or expanded grains, tablets, powder or bolus forms.

7. A method for increasing the growth rate and/or improving the feed efficiency and/or the feed conversion rate and/or the immunity of a non-human animal, the method

comprising administering to said animal an effective amount of a composition according to claims 1 - 6.

8. Use of free IAA or a derivative thereof wherein said derivative is selected from the group consisting of 4-hydroxy-IAA, 4-methoxy-IAA, 5-hydroxy-IAA, 5-methoxy-IAA, 6-hydroxy-IAA, 6-methoxy-IAA, 7-hydroxy-IAA, 7-methoxy-IAA and a compound that can be converted into free IAA in 3, preferably in 2 and more preferably in 1 step for the preparation of a therapeutical composition for stimulating the immune system in non-human animals in need of such a treatment.

9. Use of a composition according to claims 1 - 6 for the preparation of a therapeutical composition for stimulating growth and/or stimulating the immune system in animals in need of such a treatment.

10. Use according to claims 8 or 9 wherein the free IAA or a derivative thereof is capable of increasing the serum level of insulin-like growth factor 1 (IGF-1).

11. Use according to claims 8 - 10 wherein the animal has a lowered level of IGF-1.

12. Use according to claims 8 - 11 wherein the animals have a growth deficit and/or a weakened immune system.

13. Method for the preparation of an animal feed composition, said method comprising admixing a composition according to claims 1 - 6 with one or more feed substance(s)

or ingredient(s) in order to obtain an animal feed composition according to claims 1 - 6.

14. Method for the preparation of an animal feed composition, said method comprising the step of supplementing an animal feed with free IAA or a derivative thereof in order to obtain an animal feed composition according to claims 1 - 6.

15. Method for raising non-human animals comprising:

1) mixing an effective dose of free IAA or a derivative thereof with a feed material in order to obtain a feed composition according to claims 1 - 6, suitable for a particular animal species

2) feeding said species with the feed material